NeuroNEXT Network

Standard Operating Procedure (SOP)

Protocol Working Group Formation and Proposal Development

Version 1.0

SOP NN PD 302

Originators: NeuroNEXT CCC and DCC Personnel

Reviewed and Approved by:

Signature and Date: DocuSigned by Christopher Coffey Christopher Coffey | I approve this document 14-Feb-2023 | 12:36:43 PM PST C68AC8DD80334CF982AED1200765F147 14-Feb-2023
Name and Title: Christopher S. Coffey, PhD (DCC Principal Investigator)
Signature and Date: DocuSigned by Merit Cudkowicz Merit Cudkowicz | I approve this document 20-Feb-2023 | 11:41:28 AM EST 9F8FE4180E504C6AB0A67B835E80C644 20-Feb-2023
Name and Title: Merit E. Cudkowicz, MD MSc (CCC Principal Investigator)
Signature and Date: DocuSigned by Marianne Chase Marianne Chase | I approve this document 14-Feb-2023 | 9:45:15 AM EST 58FE690F6BCA4F2390E3DA15BCE3F578 14-Feb-2023
Name and Title: Marianne Chase, BA (CCC Senior Director of Clinical Trials Operations)

Signature and Date:

DocuSigned by DIXIE ECKLUND
I approve this document
15-Feb-2023 | 10:42:01 AM PST
7006AF622EFC40B6A067A08EC02591B6

15-Feb-2023

Name and Title: Dixie J. Ecklund, RN MSN MBA (DCC Associate Director)

Signature and Date:

DocuSigned by Stacey Grabert
I approve this document
22-Feb-2023 | 11:29:08 AM EST
60CC52B0747A44E6B2208D8D880698C0

22-Feb-2023

Name and Title: Stacey Grabert, Pharm.D, MS, (CCC Director of Quality Assurance)

Signature and Date:

DocuSigned by Joan Ohayon
I approve this document
14-Feb-2023 | 9:38:27 AM PST
72C6AAFD8CC4485582ACA0700072901A

14-Feb-2023

Name and Title: Joan Ohayon, RN, MSN, CRNP, MSCN (NINDS, NeuroNEXT Program Official)

NN PD 302

NEURONEXT NETWORK STANDARD OPERATING PROCEDURE FOR PROTOCOL WORKING GROUP FORMATION AND PROPOSAL DEVELOPMENT

1. POLICY

It is the policy of the NeuroNEXT Network that each proposal that is deemed by the NeuroNEXT Executive Committee (NEC) to be "feasible", and has been approved by the ESC (if needed), will proceed to a Protocol Working Group (PWG) that has been formed with the goal of developing the proposal into a full grant submission. The procedures outlined here for establishing a PWG and developing the proposal were developed in collaboration with the National Institute of Neurological Disorders and Stroke (NINDS).

2. SCOPE

The policies and procedures described in this SOP apply to the NeuroNEXT Clinical Coordinating Center (CCC) and Data Coordinating Center (DCC) within the context of their oversight and advisory roles for the NeuroNEXT Network, and to all NeuroNEXT investigators, staff, subcontractors, or other entities associated with the NeuroNEXT Network who manage, oversee, and conduct research in the Network.

3. ROLES AND RESPONSIBILITIES

The NeuroNEXT Executive Committee (NEC) is responsible for reviewing proposals that NINDS has deemed appropriate for the mission and goals of the Network, to determine if the proposal is "feasible" to be conducted in the Network. If the NEC determines that a proposal is feasible for the Network and it is approved, as needed, by the ESC, the CCC PI will work with the PPI to identify members for the PWG. For proposals deemed feasible, but requiring additional revision of the study aims, the PPI will be notified that pre-PWG consultation with one or more disease specialists in the Network to revise the study aims will be required. The PPI will be responsible for submitting a revised Proposal Concept form, reflecting the revisions discussed during the pre-PWG consultation period, to the CCC Project Manager (PM) for distribution to the full PWG prior to the first full PWG meeting.

Prior to the first full PWG meeting, appropriate members of the CCC and DCC will schedule an Introduction to the Network teleconference with the PPI to provide guidance and review Network procedures. In addition, the CCC lead clinician and DCC lead biostatistician will communicate with the PPI to review the study aims and identify key items for discussion with the full PWG.

Each PWG will consist of the Protocol Principal Investigator (PPI), appropriate members of the PPI study team, appropriate members of the CCC and DCC including a CCC Lead identified by the CCC PI (clinician) and a DCC Lead (biostatistician) identified by the DCC PI, a CCC Project Manager, appropriate subject matter experts, and a patient community advocate. PWG membership may vary depending on the needs of the study.

For proposals seeking U01 funding, representatives from industry will not be included on PWGs.

For protocols seeking U44 funding, a representative from the company will be included on the PWG, as a non-voting member.

The CCC Project Manager is responsible for facilitating and participating in PWG meetings. The CCC PI may identify and invite appropriate members of the main PWG, CCC and/or DCC to serve on subgroups or subcommittees, as required by the project. Subgroups may include Study Design, Budget, Central Pharmacy and Laboratory, Recruitment, Retention and Diversity, and Regulatory/IND submission preparation. The PPI is responsible for drafting a full Protocol preferably using the NN Protocol Template and submitting it to the CCC PM for distribution to PWG members, prior to the first full PWG meeting. If additional revisions to the Protocol are indicated based on subsequent PWG discussion(s) the PPI will provide revised Protocols as indicated.

The PPI is responsible for working with the appropriate PWG members to develop the full protocol, and working with the CCC and DCC to develop the study budget for grant submission.

The CCC and DCC are responsible for assisting the PPI with developing their grant application and full budget. The CCC and DCC leads will review components of the final grant application (i.e. Specific Aims, Research Strategy, Protocol) prior to submission, provide feedback and communicate with the NEC regarding any concerns with

providing a NEC letter of support for inclusion with the application. PWGs are disbanded once the final grant applications has been submitted.

After a grant application has been reviewed, the PWG may be reconvened, if the review summary statements raise specific points that require their assistance.

4. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 314.126	Adequate and Well-Controlled Studies
ICH E6 2.2, 2.4 – 2.6	The Principles of ICH GCP
ICH E6, 2.10, 2.11	The Principles of ICH GCP
ICH E6, 5.4	Trial Design
ICH E6, 5.23	Multicentre Trials
ICH E8	General Considerations for Clinical Trials (December 1997)
ICH E9	Statistical Principles for Clinical Trials (September 1998)
ICH E10	Choice of Control Group and Related Issues in Clinical Trials (May 2001)

5. REFERENCES TO OTHER APPLICABLE SOPS

NN GA 102	Document Development and Change Control
NN PD 301	Proposal Review, Initial Feasibility Assessment and ESC Review
NN PM 502	Clinical Trial Budget Development

6. ATTACHMENTS AND REFERENCES

NN PD 301-A	Document History

7. TERMS AND ABBREVIATIONS

The following terms and abbreviations are used in this document:

CCC	Clinical Coordinating Center at Massachusetts General Hospital
CCC PI	Clinical Coordinating Center Principal Investigator
DCC	Data Coordinating Center at The University of Iowa
DCC PI	Data Coordinating Center Principal Investigator
ESC	Extramural Science Committee
FDA	U.S. Food and Drug Administration
GCP	Good Clinical Practice
ICH	International Conference on Harmonisation
IDE	Investigational Device Exemption
IND	Investigational New Drug application
PPI	Protocol Principal Investigator
PWG	Protocol Working Group

8. SPECIFIC PROCEDURES

A. Creating a PWG

#	*Who*	*Task*	*Attachment/ References*	*Related SOP*
1.	CCC/DCC PI	For a proposal deemed feasible by the NEC, but requiring revision of study aims, notify the PPI that pre-PWG consultation with Network disease experts will be required prior to the first full PWG meeting.		
2.	PPI of proposals requiring pre-PWG consultation	Revise Protocol Concept form based on pre-PWG consultation and submit to CCC PM for distribution to PWG members prior to first full PWG meeting.		
3.	CCC PI in consultation with PPI	Identify and invite appropriate members to serve on the PWG.		
4.	CCC PI or designee	Initiate scheduling of full PWG meetings, and provide members with objectives.		
5.	CCC and DCC representatives	Conduct Introduction to the Network teleconference with PPI prior to first full PWG meeting.		
6.	PPI, CCC and DCC leads	Prior to full PWG, as needed, communicate regarding study aims and key items for full PWG discussion.		
6.	CCC PI or designee	Identify and invite appropriate members to serve on subgroups or subcommittees, as required by the project.		

B. Proposal Development

#	*Who*	*Task*	*Attachment/ References*	*Related SOP*
1.	CCC	Schedule initial PWG meeting, additional PWG meetings as needed, and appropriate subcommittee meetings.		
2.	DCC	Schedule study design subcommittee meetings.		
3.	PPI	Work with appropriate PWG members to refine and revise study objectives and statistical design parameters, as needed.		
4.	PPI	Work with appropriate PWG members to determine drug/pharmacy/central laboratory needs and issues for study, as needed.		
5.	PPI	Provide Schedule of Assessments and any other budgetary requirements for study to appropriate PWG members, and assist in creation of draft study budget.		NN PM 502
6.	PPI	Once members of the PWG have agreed upon final study design, prepare a presentation of the study for the Network CSS		

#	*Who*	*Task*	*Attachment/ References*	*Related SOP*
7.	CCC	Schedule PPI presentation to the Network and notify all Network CSS		
8.	PPI	Develop study specific questionnaire, to be completed by each CSS, with questions related to feasibility and logistics of conducting the study at their CSS		
9.	CCC	Distribute study specific questionnaire and other required materials to each CSS		
10.	CCC	Collect all materials from CSS and provide information to PPI as agreed upon		
11.	CCC, DCC	Schedule and conduct calls with the PPI to provide guidance on the grant application process, including development of the detailed budget and justification.		
12.	PPI	Follow all Network guidelines in preparing the initial draft grant application, detailed budget and justification and provide them to appropriate members of the PWG and all NEC members for review		SOP 303
13.	CCC and DCC PWG leads	Review near final version of the Specific Aims, Research Strategy and Protocol, provide feedback to PPI and communicate with NEC regarding any concerns with providing a NEC letter of support for inclusion with the application		
14.	CCC	Notify PWG members that their PWG has disbanded once final grant application is submitted		
15.	CCC and DCC	Once summary review statements are received on grant applications, work with the PPI to determine whether or not there are any specific points that require the PWG to reconvene		

DocuSign

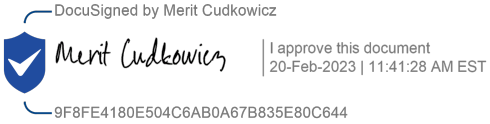
Certificate Of Completion

Envelope Id: 470519AEF9E44ACF8DB12D28CD8A0C31
Status: Completed
Subject: Complete with DocuSign: NN PD 302 PWG Formation and Proposal Development V1.0.docx
Source Envelope:
Document Pages: 6
Signatures: 6
Envelope Originator:
Certificate Pages: 6
Initials: 0
Tania Leeder
AutoNav: Enabled
TLEEDER@PARTNERS.ORG
EnvelopeId Stamping: Disabled
IP Address: 73.123.188.5
Time Zone: (UTC-05:00) Eastern Time (US & Canada)

Record Tracking

Status: Original
2/14/2023 9:36:23 AM
Holder: Tania Leeder
TLEEDER@PARTNERS.ORG
Location: DocuSign

Signer Events	Signature	Timestamp
Christopher Coffey christopher-coffey@uiowa.edu Security Level: Email, Account Authentication (Required), Login with SSO	 Signature Adoption: Pre-selected Style Signature ID: C68AC8DD-8033-4CF9-82AE-D1200765F147 Using IP Address: 128.255.113.139 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	Sent: 2/14/2023 9:38:29 AM Viewed: 2/14/2023 3:36:33 PM Signed: 2/14/2023 3:36:46 PM
Electronic Record and Signature Disclosure: Accepted: 2/14/2023 3:36:33 PM ID: fbd97b8f-409b-48ec-9d3b-dd6ac0447986		
DIXIE ECKLUND dixie-ecklund@uiowa.edu Security Level: Email, Account Authentication (Required), Login with SSO	 Signature Adoption: Drawn on Device Signature ID: 7006AF62-2EFC-40B6-A067-A08EC02591B6 Using IP Address: 128.255.112.230 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	Sent: 2/14/2023 9:38:30 AM Viewed: 2/15/2023 1:37:31 PM Signed: 2/15/2023 1:42:03 PM
Electronic Record and Signature Disclosure: Accepted: 2/15/2023 1:37:31 PM ID: eaf788ad-51c2-4553-93a8-828b3666650a		

Signer Events	Signature	Timestamp
Joan Ohayon ohayonj@ninds.nih.gov Security Level: Email, Account Authentication (Required)	 Signature Adoption: Pre-selected Style Signature ID: 72C6AAFD-8CC4-4855-82AC-A0700072901A Using IP Address: 156.40.137.188 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	Sent: 2/14/2023 9:38:32 AM Viewed: 2/14/2023 12:38:14 PM Signed: 2/14/2023 12:38:31 PM
Electronic Record and Signature Disclosure: Accepted: 2/13/2023 2:03:22 PM ID: 385a0a53-0f0c-4395-88f6-d5700c36e050		
Marianne Chase MCHASE@mgh.harvard.edu Sr Director, Clinical Trial Operations Insight OBO The Massachusetts General Hospital Security Level: Email, Account Authentication (Required), Logged in	 Signature Adoption: Pre-selected Style Signature ID: 58FE690F-6BCA-4F23-90E3-DA15BCE3F578 Using IP Address: 73.114.253.109 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	Sent: 2/14/2023 9:38:30 AM Viewed: 2/14/2023 9:44:50 AM Signed: 2/14/2023 9:45:19 AM
Electronic Record and Signature Disclosure: Not Offered via DocuSign		
Merit Cudkowicz cudkowicz.merit@mgh.harvard.edu Chief of Neurology Security Level: Email, Account Authentication (Required)	 Signature Adoption: Pre-selected Style Signature ID: 9F8FE418-0E50-4C6A-B0A6-7B835E80C644 Using IP Address: 68.239.56.73 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	Sent: 2/14/2023 9:38:31 AM Viewed: 2/20/2023 11:41:18 AM Signed: 2/20/2023 11:41:31 AM
Electronic Record and Signature Disclosure: Accepted: 2/20/2023 11:41:18 AM ID: 4d04bc70-1540-4640-82c6-cf6ceec8f994		

Signer Events	Signature	Timestamp
Stacey Grabert sgrabert@mgh.harvard.edu Director QA Stacey Grabert Security Level: Email, Account Authentication (Required)	 Signature Adoption: Pre-selected Style Signature ID: 60CC52B0-747A-44E6-B220-8D8D880698C0 Using IP Address: 132.183.56.49 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	Sent: 2/14/2023 9:38:31 AM Viewed: 2/22/2023 11:28:58 AM Signed: 2/22/2023 11:29:11 AM
Electronic Record and Signature Disclosure: Accepted: 7/20/2020 8:50:14 AM ID: 5ebadf74-e399-40fd-be82-9c7ca902061b		

In Person Signer Events	Signature	Timestamp

Editor Delivery Events	Status	Timestamp

Agent Delivery Events	Status	Timestamp

Intermediary Delivery Events	Status	Timestamp

Certified Delivery Events	Status	Timestamp

Carbon Copy Events	Status	Timestamp

Witness Events	Signature	Timestamp

Notary Events	Signature	Timestamp

Envelope Summary Events	Status	Timestamps
Envelope Sent	Hashed/Encrypted	2/14/2023 9:38:32 AM
Certified Delivered	Security Checked	2/22/2023 11:28:58 AM
Signing Complete	Security Checked	2/22/2023 11:29:11 AM
Completed	Security Checked	2/22/2023 11:29:11 AM

Payment Events	Status	Timestamps

Electronic Record and Signature Disclosure

ELECTRONIC RECORD AND SIGNATURE DISCLOSURE

From time to time, Insight OBO The Massachusetts General Hospital (we, us or Company) may be required by law to provide to you certain written notices or disclosures. Described below are the terms and conditions for providing to you such notices and disclosures electronically through the DocuSign system. Please read the information below carefully and thoroughly, and if you can access this information electronically to your satisfaction and agree to this Electronic Record and Signature Disclosure (ERSD), please confirm your agreement by selecting the check-box next to 'I agree to use electronic records and signatures' before clicking 'CONTINUE' within the DocuSign system.

Getting paper copies

At any time, you may request from us a paper copy of any record provided or made available electronically to you by us. You will have the ability to download and print documents we send to you through the DocuSign system during and immediately after the signing session and, if you elect to create a DocuSign account, you may access the documents for a limited period of time (usually 30 days) after such documents are first sent to you. After such time, if you wish for us to send you paper copies of any such documents from our office to you, you will be charged a $0.00 per-page fee. You may request delivery of such paper copies from us by following the procedure described below.

Withdrawing your consent

If you decide to receive notices and disclosures from us electronically, you may at any time change your mind and tell us that thereafter you want to receive required notices and disclosures only in paper format. How you must inform us of your decision to receive future notices and disclosure in paper format and withdraw your consent to receive notices and disclosures electronically is described below.

Consequences of changing your mind

If you elect to receive required notices and disclosures only in paper format, it will slow the speed at which we can complete certain steps in transactions with you and delivering services to you because we will need first to send the required notices or disclosures to you in paper format, and then wait until we receive back from you your acknowledgment of your receipt of such paper notices or disclosures. Further, you will no longer be able to use the DocuSign system to receive required notices and consents electronically from us or to sign electronically documents from us.

All notices and disclosures will be sent to you electronically

Unless you tell us otherwise in accordance with the procedures described herein, we will provide electronically to you through the DocuSign system all required notices, disclosures, authorizations, acknowledgements, and other documents that are required to be provided or made available to you during the course of our relationship with you. To reduce the chance of you inadvertently not receiving any notice or disclosure, we prefer to provide all of the required notices and disclosures to you by the same method and to the same address that you have given us. Thus, you can receive all the disclosures and notices electronically or in paper format through the paper mail delivery system. If you do not agree with this process, please let us know as described below. Please also see the paragraph immediately above that describes the consequences of your electing not to receive delivery of the notices and disclosures electronically from us.

How to contact Insight OBO The Massachusetts General Hospital:

You may contact us to let us know of your changes as to how we may contact you electronically, to request paper copies of certain information from us, and to withdraw your prior consent to receive notices and disclosures electronically as follows:
To contact us by email send messages to: jhenrique@mgh.harvard.edu

To advise Insight OBO The Massachusetts General Hospital of your new email address

To let us know of a change in your email address where we should send notices and disclosures electronically to you, you must send an email message to us at jhenrique@mgh.harvard.edu and in the body of such request you must state: your previous email address, your new email address. We do not require any other information from you to change your email address.

If you created a DocuSign account, you may update it with your new email address through your account preferences.

To request paper copies from Insight OBO The Massachusetts General Hospital

To request delivery from us of paper copies of the notices and disclosures previously provided by us to you electronically, you must send us an email to jhenrique@mgh.harvard.edu and in the body of such request you must state your email address, full name, mailing address, and telephone number. We will bill you for any fees at that time, if any.

To withdraw your consent with Insight OBO The Massachusetts General Hospital

To inform us that you no longer wish to receive future notices and disclosures in electronic format you may:

i. decline to sign a document from within your signing session, and on the subsequent page, select the check-box indicating you wish to withdraw your consent, or you may;

ii. send us an email to jhenrique@mgh.harvard.edu and in the body of such request you must state your email, full name, mailing address, and telephone number. We do not need any other information from you to withdraw consent.. The consequences of your withdrawing consent for online documents will be that transactions may take a longer time to process..

Required hardware and software

The minimum system requirements for using the DocuSign system may change over time. The current system requirements are found here: https://support.docusign.com/guides/signer-guide-signing-system-requirements.

Acknowledging your access and consent to receive and sign documents electronically

To confirm to us that you can access this information electronically, which will be similar to other electronic notices and disclosures that we will provide to you, please confirm that you have read this ERSD, and (i) that you are able to print on paper or electronically save this ERSD for your future reference and access; or (ii) that you are able to email this ERSD to an email address where you will be able to print on paper or save it for your future reference and access. Further, if you consent to receiving notices and disclosures exclusively in electronic format as described herein, then select the check-box next to 'I agree to use electronic records and signatures' before clicking 'CONTINUE' within the DocuSign system.

By selecting the check-box next to 'I agree to use electronic records and signatures', you confirm that:

- You can access and read this Electronic Record and Signature Disclosure; and
- You can print on paper this Electronic Record and Signature Disclosure, or save or send this Electronic Record and Disclosure to a location where you can print it, for future reference and access; and
- Until or unless you notify Insight OBO The Massachusetts General Hospital as described above, you consent to receive exclusively through electronic means all notices, disclosures, authorizations, acknowledgements, and other documents that are required to be provided or made available to you by Insight OBO The Massachusetts General Hospital during the course of your relationship with Insight OBO The Massachusetts General Hospital.